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Nephrology

AN INTERESTING CASE OF FIRE ANT BITE CAUSING HEMOLYTIC UREMIC SYNDROME

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ABSTRACT **Background** Hemolytic-uremic syndrome (HUS) is a severe, life-threatening condition characterized by symptoms such as hemolytic anemia, renal failure, and a low platelet count. Bacterial infections, medicine, post-hematopoietic cell transplantation, pregnancy, autoimmune illness, and acquired immunodeficiency syndrome are all potential causes. **Case presentation** We report the case of a 40-year-old healthy man who developed acute renal failure caused by HUS. Typical symptoms of HUS combined with severe uremia developed after a large local reaction after suspected Solenopsis fire ant bites. He was successfully treated with plasma exchange and achieved a complete recovery of renal function. **Conclusion** This is a rare case demonstrating a major systemic reaction of HUS to ant bites, highlighting this severe consequence in individuals exposed to fire ant bites.

KEYWORDS : Haemolytic-uremic syndrome, Plasma exchange, Renal failure, Venomous insects.

INTRODUCTION

Hemolytic-uremic syndrome (HUS) is a disease commonly preceded by E. coli O157:H7 or other Shiga toxin-producing bacterial infections, medication (chemotherapy agents, cyclosporine, tacrolimus, quinine, ticlopidine, etc.), post-hematopoietic cell transplantation, pregnancy, autoimmune diseases (APLA, systemic lupus erythematosus, scleroderma renal crisis), acquired immuno deficiency syndrome, and idiopathic form of HUS.

A 40-year-old man had acute renal failure and HUS after a significant local response on the right leg caused by fire ant bites in our case. This rare example indicates a link between HUS and fire ant bites. The mechanisms of HUS produced by fire ant venom are thoroughly discussed.

Case Presentation

A 40-year-old healthy male tribe who travels into the Nallamalla reserve forest on a daily basis to collect firewood, which is his main source of income. He had been bitten by red ants 14 days before being admitted to the hospital. An immediate flare and wheal formed across the right leg, followed by erythematous, oedematous, and indurated responses. In just two days, he had a high grade fever. He was treated at a rural medical practitioner, and the local response faded gradually. However, 5 days later, he began vomiting violently. His urine production likewise significantly reduced. He was taken to a nearby hospital for treatment, where he was given intravenous fluids before being transported to GGH Kurnool.

Physical examination indicated a pulse rate of 86 beats per minute, blood pressure of 160/90 mmHg, body temperature of 37°C, and respiration rate of 21 breaths per minute at the time of presentation. Mild obesity (body mass index, 28.2 kg/m2) and pale conjunctivae were among the relevant positive results. There was no oedema, icteric sclera, abdominal mass, or visibly enlarged kidney.

Laboratory data on admission showed the following values:

serum sodium: 138mEq/L; potassium:3.8 mEq/L; urea nitrogen: 151 mg/dL; creatinine: 20.1 mg/dL; calcium: 8.4 mg/dL; phosphorus: 3.9 mg/dL; albumin: 4.2 g/dL; aspartate aminotransferase: 127 U/L; alanine aminotrans- ferase: 36 U/L; total bilirubin: 5.9 g/dL; direct bilirubin: 2.4 g/dL; uric acid: 19.1 g/dL; myoglobin: 422 ng/mL; lactate dehydrogenase: 1760 U/L; creatine kinase (CK): 503 U/Troponin: 0.01 µg/L; and haptoglobin <7.0 mg/dL. Arterial blood gases revealed a pH of 7.26, pCO2 of 41 mmHg, pO2 of 91 mmHg, oxygen saturation of 97.4%, and bicarbonate level of 18 mEq/L. Complete blood count (CBC) showed the levels of haemoglobin at 8.2 g/dL, white blood cells (WBC) at 13.9 × 10^3/µL, platelets at 57 x 10^3/µL, and a high reticulocyte level at 6.8%. WBC differential count showed neutrophils at 79.5%, eosinophils at 2.7%, basophils at 0.4%, and monocytes at 6.8%. Both prothrombin time and partial thromboplastin time were within normal ranges. Direct and indirect Coombs tests were both negative. A peripheral blood smear revealed normocytic normochromic RBC and few schistocytes noted in high-power field.

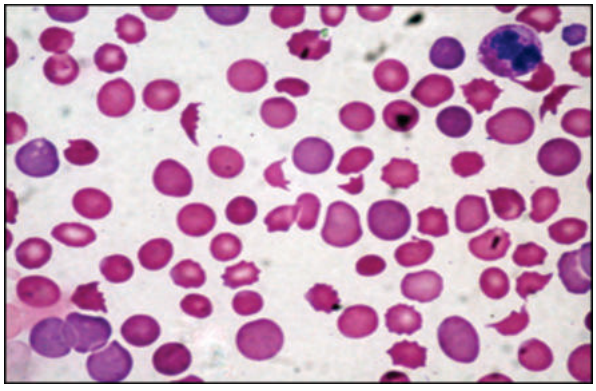

Figure.1 Peripheral blood smear showing schistocytes.

Immunoglobulin (Ig) G, IgA, and IgM levels were all within normal ranges, but IgE level was high at 406.0 IU/mL. Serum complement showed the C3 level at 129 mg/dL (normal range, 90–180 mg/dL), and the C4 level at 33.2 mg/dL (normal range, 10–40 mg/dL). The serum antinuclear antibody level was within the normal range. Results for venereal disease research laboratory, hepatitis B surface antigen (HBsAg), hepatitis C, and human immunodeficiency virus antibodies were all negative. Urinalysis revealed dark brown urine with 3+ protein, 2–3 red blood cells, and 3–5 white blood cells per high-power field, with positive results for haemoglobin. Renal ultrasound showed normal echotexture in both kidneys with right and left renal size at 12.4 × 6.45 cm and 12.5 × 6.4 cm, respectively.

The patient was diagnosed with acute renal failure related to HUS and was treated for 6 days with plasma exchange at one plasma volume per day. For oliguria and uremic symptoms such as nausea, vomiting, and dyspnoea, haemodialysis was also started. The patient had haemodialysis every other day for a total of six sessions. Blood samples for bacteria were negative, as were stool cultures for E. coli O157. On the seventh day of stay, an echo-guided kidney biopsy was conducted. Pathological investigation revealed a partly collapsed glomerulus, endothelial cell enlargement, subendothelial expansion with fluffy debris, and glomerular basement membrane double-contour development, and intra capillary thrombi, all of which are consistent with HUS.

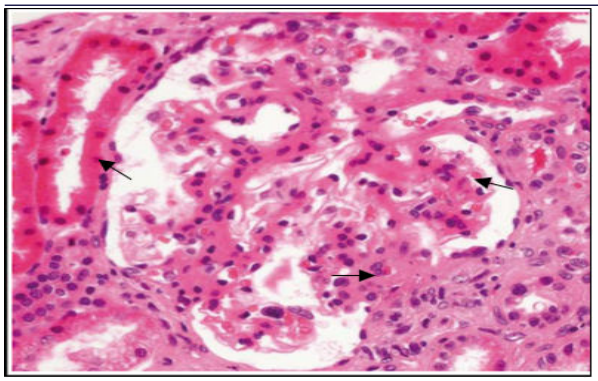

Figure.2 Kidney Biopsy suggesting HUS

The patient's urine production and renal function improved further after plasma exchange, haemodialysis, and supportive therapy. Simultaneously, haemolytic anaemia and thrombocytopenia gradually recovered, and dialysis was discontinued on day 8 of hospitalization. Finally, with a creatinine level of 1.9 mg/dL, the patient was discharged. The patient was in good health at the one-month follow-up examination, with normal renal function and CBC. He was still on antihypertensive medicines (amlodipine 5 mg OD, carvedilol 25 mg OD) 1 year after discharge due to chronic hypertension (blood pressure about 140/90 mmHg).

DISCUSSION

Historically, the Red fire ant (Solenopsis) is coppery-brown on the head and body with darker abdomen. The fire ant venom is complex, with numerous proteins capable of causing allergy and anaphylaxis. In addition to these proteins, piperidine alkaloids are present and constitute a significant portion of fire ant venom (about 95%) [1]. This component is not allergic, but it is responsible for the local discomfort and pustules that are frequent with ant bites. Fire ant bites can cause three types of reactions: local, big local, and systemic (anaphylaxis) [2-5]. A local response causes an instantaneous flare and wheal, which is followed by a pustule after about a day. A big local response is characterized by an erythematous, oedematous, and indurated zone that extends beyond the pustule and can remain for several days. The prevalence of significant systemic responses is substantially lower, at around 2%. The ant venom's biological activity generates cytotoxic, neurotoxic, and haemolytic effects within the body [6,7]. It also promotes coagulation and makes the person hypercoagulable [8-10]. In 1993, Javors et al. reported that alkaloids included in fire ant venom influence various physiological and biochemical processes of human platelets and neutrophils [10]. He discovered that venom alkaloids stimulated platelet intracellular calcium ion concentration (Ca^{2+}), dense granule secretion, and aggregation. The platelet-activating factor (PAF) response was less complete. Furthermore, pre-treatment of platelets with venom alkaloids resulted in increased PAF-related intracellular Ca^{2+} spiking, indicating a synergistic effect between the two agonists.

In addition, venom alkaloids stimulate and accumulate neutrophils and intracellular Ca^{2+}. These findings imply that alkaloids included in fire ant venom activate platelets and neutrophils. Platelet thrombi development and endothelial damage may occur in vivo as a result of fire ant bites. In fact, a 5-day-old neonate developed microangiopathic haemolytic anaemia after being bitten by a fire ant [11].

These findings may help to understand how HUS develops after being exposed to fire ant venom. There have been some case reports of HUS or ADAMTS-13 insufficiency following scorpion stings [12-15], but to the best of our knowledge, there have been only few reports of HUS development following ant bites.

The drawback of our findings is that we cannot investigate complement regulators, genetic alterations, or ADAMTS 13 activity in this patient. As a result, the probability of atypical HUS and TTP cannot be ruled out totally. The diagnosis of atypical HUS is largely one of exclusion, based on evidences of microangiopathic haemolytic anaemia (MAHA), thrombocytopenia, and renal failure in the absence of infections by Shiga-toxin producing bacteria or other microorganisms associated with HUS, of possible causes of secondary forms of HUS (such as medications, autoimmune diseases, and malignancy), and of reduced ADAMTS 13 activity (10%) [16]. Atypical HUS denotes a primary illness caused by a defect in complement alternative route control. The onset ranges from neonatal to adult [16,17]. Approximately one-third of HUS patients have progressed to end-stage renal disease, and half have relapsed. Gene mutations in complement regulating proteins thrombomodulin, factor H, factor I, and membrane cofactor protein (MCP) have been discovered. Mutations in the genes encoding C3 convertase proteins, C3 and factor B, as well as patients with anti-factor H antibodies, have also been documented [16,17].

Around 20% of pedigrees have the illness. Recent research has shown that complement abnormalities, such as low C3 levels, which indicate activation of the complement alternative route, are observed only in a subgroup of patients and are not required to make the diagnosis of atypical HUS [16,18]. Despite the fact that our patient did not have a family history of HUS and had normal serum C3, C4 levels, we cannot rule out a hypothetical involvement of complement dysregulation in the aetiology of this case. ADAMTS 13 activity is frequently reduced or absent in individuals with thrombotic thrombocytopenic purpura (TTP), and it is a useful diagnostic for distinguishing TTP from atypical HUS.

A case report of ADAMTS 13 deficiency following a scorpion bite and complete recovery after plasma exchange therapy has been published [19]. Furthermore, a persistent minority of individuals with severe ADAMTS13 deficiency exhibits no neurological symptoms (e.g., 29% in the series of 65 patients from the Oklahoma TTP-HUS Registry published by JN George) [19]. Because the clinical aspects of TTP are comparable to those of our case, we believe that even though our patient did not have any neurologic symptoms (such as headache, dysphasia, seizure, confusion, stupor, or coma), TTP is a viable differential diagnosis until normal ADAMTS13 activity is demonstrated.

CONCLUSION:

We provide a fresh case report of HUS and abrupt renal failure caused by fire ant bites. The ant venom alkaloids may be responsible for platelet and neutrophil activation, platelet thrombi formation, endothelial damage, and, eventually, the development of HUS. Although the likelihood of atypical HSU and TTP cannot be totally ruled out, this case depicts a significant systemic reaction of HUS to fire ant bites and highlights the importance of being aware of this complication in patients who experience fire ant bites.

Consent:

The patient gave written informed consent for the publishing of this case report and related photos.

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